REMARKS

Claims 1, 4-7 and 23 are pending in the application. In the present amendment claims 1 and 23 have been amended to recite that the condition to be treated is an epileptic condition. Support for this amendment is found in the specification and claims as originally filed, for example, at page 68, lines 28-29 and Fig. 2B.

No new matter is introduced by way of the claim amendments.

Priority

The full-length trkC sequence of SEQ ID NO: 6 is found in the priority application Serial No. 08/215,139 filed on March 18, 1994. The use of trkC antibodies for the treatment of axonal sprouting in epilepsy is also mentioned (*e.g.*, page 88, lines 6-7). The claims of the present application are directed to use of trkC antibodies for the treatment of axonal sprouting in epilepsy. Accordingly, applicants submit that the priority date of the present application is March 18, 1994.

Rejections

Claims 1, 4-7, and 23 stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. Claims 1, 4-7, and 23 stand rejected for alleged lack of written description. These rejections are respectfully traversed.

The Rejections of Claims 1, 4-7, and 23 Under 35 U.S.C. §112, First Paragraph for Alleged Lack of Enablement

Claims 1, 4-7, and 23 stand rejected as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

The Examiner reviews prior rejections and arguments regarding these rejections (pages 4-9, Office Action mailed October 18, 2005). The Examiner suggests that "the specification provides no

teaching or guidance drawn to the non-productive receptors and their sequestration of the antagonist antibody" and suggests that thus "it cannot be predicted whether sufficient antibody would bind human trkC receptor of SEQ ID NO:6 to function as claimed" (page 3, lines 7-11, Office Action mailed October 18, 2005). The Examiner further suggests that "[i]n the absence of this guidance, one would not know how to predictably distinguish between antagonist antibody that would selectively antagonize the activity of SEQ ID NO:6 and therefore would not be sequestered by truncated or variant forms of the receptor and thus would function as claimed" (page 4, lines 13-17, Office Action mailed October 18, 2005).

Applicants note that the present claims are directed to inhibiting the activity of active full-length trkC receptors (in order to inhibit their activity, the full-length trkC receptors must be active receptors). A trkC receptor without activity, such as a "non-productive receptor," or an inactive variant form, would not be inhibited, being already inactive. A truncated trkC receptor would not be a "full-length trkC receptor." Accordingly concerns related to truncated or variant forms, or forms arising by alternate splicing, or non-productive receptors are believed to be moot in view of the present claims directed to inhibiting the activity of the full-length trkC receptor of SEQ ID NO: 6.

Applicants have discussed such concerns in prior amendments, noting, for example, that it is well within the skill of one of ordinary skill in the art to increase an applied dose if it happens that there is indeed sequestration of antibody by "variant forms of the receptor" or other ineffective or non-specific binding. Dosages are discussed in the specification as filed (see, e.g., page 70, lines 20-28). Although the Examiner suggests that "undue experimentation" would be required, Applicants submit that it is clear that one of ordinary skill in the art would know how to determine an effective dosage, and that such a determination was routine in the art at the time the application was filed, and would not require an undue amount of experimentation.

In addition, Applicants note that, in arguments addressed to a related point, the Examiner stated that "it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*" (page 7, lines 19-20, Office Action mailed October 18, 2005). However, the Examiner has presented no data demonstrating such an effect *in vivo* as the suggested sequestration

"by truncated or variant forms of the receptor." No such data is presented in the present specification. In view of the "recognized" differences between "cultured cells and their counterparts *in vivo*" and the Examiner's arguments related to such differences, it is clear that the Examiner must present *in vivo* data to support the contention that such a sequestration effect might be expected *in vivo*. In the absence of such data, or of general knowledge in the art of such an effect of truncated or variant forms of SEQ ID NO:6, Applicants submit that the rejection lacks a proper basis.

The Examiner discussed arguments related to the utility of the present invention in treating aberrant neuronal sprouting and epilepsy. Applicants note that the claims are explicitly directed to methods for treating aberrant neuron sprouting in epilepsy. Accordingly, the Examiner's comments suggesting that the arguments were directed to "limitations not recited in the claims as currently constituted" (e.g. page 4, lines 5-6, 15-16, and 24-25) are believed to be moot.

As discussed in previous responses (which are hereby incorporated by reference to avoid unnecessary duplication of argument), it was recognized in the art that neuronal sprouting occurred in epilepsy, that there was a relationship between NT-3 and neuronal sprouting (and thus a relationship between NT-3 and epilepsy), and that there was a relationship between trkC and epilepsy. This recognition in the art at the time the application was filed, taken with the statement in the specification at page 68, lines 24-29 that "[t]his antagonist activity is believed to be useful in the treatment of pathological conditions associated with endogenous neurotrophin production, such as ... aberrant sprouting in epilepsy ..." would be understood by one of ordinary skill in the art to provide an explicit connection between a full-length trkC receptor of SEQ ID NO: 6, aberrant neuronal sprouting, and a disease (epilepsy).

Applicants note that the claims are explicitly directed to treating aberrant neuronal sprouting in epilepsy. Applicants note that the specification directly and explicitly discloses that the invention is useful in treating epilepsy. Moreover, it was recognized in the art at the time that aberrant sprouting was related to epilepsy, and that aberrant sprouting might be affected by neurotrophin levels and neurotrophin receptor activty. The disclosure in a patent specification is addressed to one of skill in the art; such a skilled person, with their knowledge of the art, reading the specification would have immediately recognized and appreciated the connection between inhibition of the

activity of a trkC receptor of SEQ ID NO: 6 and the treatment of epilepsy. Accordingly, a nexus was established between a trkC of SEQ ID NO: 6 and aberrant sprouting in epilepsy, and would have been recognized as such by one of ordinary skill in the art.

The Examiner discusses the Hongo Declaration, and argues that protein levels do not correlate with steady-state mRNA levels (pages 4-9, Office Action mailed October 18, 2005). However, as noted by the Examiner, the "the data presented in the Hongo Declaration is not drawn to RNA, but rather is drawn to protein assays" (pages 4-5, Office Action mailed October 18, 2005). The protein data discussed in the Hongo Declaration shows that the antibodies recited in the claims have the required activity. Thus, the Hongo Declaration further demonstrates the activity of the antibodies of the claims, and provides corroboration of the utility of the claimed invention.

The Examiner discusses the McNamara reference, noting that McNamara concludes that trkC, NGF and BDNF "may form part of the molecular machinery responsible for pathologic morphologic rearrangements" (page 6, lines 1-3 of the Office action dated 3/28/2005), placing particular emphasis on the word "may." The Examiner then goes on to suggest that it was "unknown to McNamara at the time the reference was published that trkC was involved in pathologic morphologic rearrangements and ... one would not know how to use the claimed invention" (page 6, lines 16-21). However, Applicants note that the clear conclusion of McNamara that trkC may be involved in pathologic morphologic rearrangements was acknowledged by the Examiner, despite the emphasis on the word "may," and despite the teachings of the other references discussed in the previous response. Such a conclusion, even including the word "may," in view of the present specification, teaches one of ordinary skill in the art how to use the claimed invention.

In addition, Applicants note that Hongo states that "Trk-specific antibodies ... find use in the treatment of diseases characterized by neurotrophin or Trk receptor expression as determined by mRNA or protein assessment" (Declaration of Hongo, page 5, lines 11-13). These remarks were directed to treatment of diseases such as those discussed in the "Specification at page 4, lines 6-10, and page 68, lines 18-29": e.g., aberrant neuronal sprouting (page 68, lines 28-29). Accordingly, Applicants believe that the Specification, references and the Declaration support the present claims.

The Examiner suggests that "Applicant neglects to address the issue raised drawn to the heterogeneity of epilepsies and the lack of teaching in the specification as to how to determine the patient population that would predictably benefit from the instantly claimed method" (page 6, lines 22-24 to page 7, line 1, Office Action mailed October 18, 2005). However, as amended, the claims are directed to aberrant neuron sprouting in epilepsy, the treatment requiring contacting epileptic neuronal cells expressing full-length human trkC receptor proteins of SEQ ID NO:6. Thus, the claims are directed to specific cells (epileptic neuronal cells expressing full-length human trkC receptor proteins of SEQ ID NO:6) in a specific population of patients (those patients suffering from an epileptic condition comprising aberrant neuron sprouting, and having epileptic neuronal cells expressing full-length human trkC receptor proteins of SEQ ID NO:6). As discussed above, inhibition of aberrant sprouting would be expected to provide benefit to human epilepsy patients suffering from a condition comprising aberrant neuronal sprouting in epilepsy. Thus, such human epilepsy patients form a patient population that would predictably benefit from the instantly claimed method. The claims being directed to an explicitly defined population, which would predictably derive benefit from the methods, Applicants believe this objection to be overcome.

The claims require that an antagonistic antibody of the invention be capable of specifically binding to a sequence within the amino acid residues 32 and 839 of SEQ ID NO: 6. The specification teaches such trkC receptors; as discussed above, such receptors would have been expected to be related to aberrant neuronal sprouting in epilepsy, and so antagonizing such receptors would be expected to be useful and effective in such treatment. The specification provides guidance for such treatments, for example, at pages 69-71. Applicants submit that one of ordinary skill in the art, following the teachings of the specification, in view of the state of knowledge in the field, would have been enabled to make and use the invention without undue experimentation. Accordingly, Applicants respectfully submit that the rejections of claims 1, 4-7 and 23 under 35 U.S.C. § 112, first paragraph as allegedly not enabled are overcome.

The Rejections of Claims 1, 4-7, and 23 Under 35 U.S.C. §112, First Paragraph for Alleged Lack of Written Description

Claims 1, 4-7, and 23 stand rejected for alleged lack of written description in the specification. The rejection of the remaining claims is respectfully traversed.

The Examiner suggests that the specification does not provide "a written description of the population of cells to be treated." (page 9, lines 21-22 of the Office Action dated 10/18/2005). However, as amended, the claims are directed to methods for inhibiting aberrant neuron sprouting in epilepsy *in vivo* in epileptic neuronal cells. Thus, the population of cells to be treated is explicitly defined in the claims, and is a population of cells that is explicitly supported in the specification (see, e.g., page 68, lines 28-29).

Accordingly, Applicants respectfully submit that the specification provides an adequate written description of the claimed invention, and that the rejections of claims 1, 4-7, and 23 under 35 U.S.C. § 112, first paragraph for alleged lack of written description are overcome.

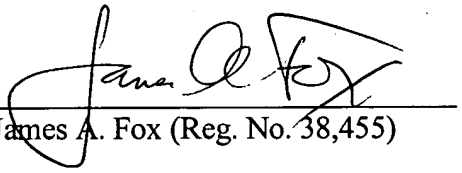
CONCLUSION

All claims pending in this application are believed to be in prima facie condition for allowance, and an early action to that effect is respectfully solicited.

Please charge the fee for a one-month extension of time, and any other fees due, including any additional fees for extension of time, or credit overpayment to Deposit Account No. **08-1641** (**Attorney's Docket No. 39766-0033 CPC4C**).

Respectfully Submitted,

Date: January 23, 2006

By: 
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